REMARKS

Claims 246-252, 255, 257-260 and 264-270 are pending in the application. Claims 257-260 and claims 268-270 have been canceled. Claim 246 has been amended to more distinctly claim that which Applicants regard as the invention and advance prosecution. Amended claim 246 is supported by the specification in Figures 2-4 and in Examples 3 and 4 (pages 124-126). Claims 264 and 265 were amended to correct dependencies. Applicants reserve the right to file subsequent continuation and/or divisional applications on canceled subject matter.

New claims 271-274 have been added to recite specific embodiments. Specifically, claim 271 recites that the construct is double stranded and that just on of the strands comprises a modified nucleotide, nucleotide analog or combination of the foregoing and that the non-nucleic acid entity is either a polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing. Claim 271 is supported by the specification in Figure 3 and on pages 36 and 126 (Example 4). Claim 272 depends from claim 271. Claim 273 recites that the construct comprises a tail and further that the tail is bound to a complementary nucleic acid sequence. The complementary nucleic acid sequence comprises non-nucleic acid entities. Claim 273 is supported by the specification in Figure 6 and Example 6. Claim 274, which depends from claim 246, recites that the construct also comprises a modified nucleotide or nucleotide analog that comprises a nuclear localization signal. Claim 274 is supported by the specification in Figure 2 and Example 3.

I. Substance of Interview

Applicants wish to thank Examiner Wollenberger for his time and helpful suggestions during his telephonic interview with the undersigned, the Examiner's representative, Cheryl H. Agris and one of the inventors, Dr. James Donegan on June 26, 2008. The substance of the interview is discussed below.

A. Brief Description of any Exhibit Shown or any Demonstration Conducted

Applicants submitted Figures 1-4.

B. Identification of Claims Discussed

Claims 246 and proposed new claims were discussed.

C. Identification of Specific Prior Art Discussed

As will be set forth in further detail below, Craig et al., US Patent No. 5,766,902 ("Craig"); Low, US Patent No. 5,108,921 ("Low"); Olsen et al., 1990, Proc. Natl. Acad. Sci. USA ("Olsen") and Hirsch et al., 1993, Transplantation Proceedings 25:138-139 ("Hirsch").

D. Identification of Principal Proposed Amendments of a Substantive Nature Discussed

The amendment of claim 246 specifically reciting that at least one modified nucleotide or at least one nucleotide analog comprises a non-fusogenic protein ligand and at least one modified nucleotide or nucleotide analog comprises a fusogenic protein was discussed. Furthermore, three proposed new claims were discussed. The first proposed new claim recited that the construct was double stranded, the non-nucleic acid entity was just on one strand and the non-nucleic acid entity was a polypeptide, a protein, a saccharide, a fatty acid, and/or a fatty acid ester and conferred cell targetting. The second proposed new claim depends on the first proposed new claim; it recites that the non-nucleic acid entity may further confer cellular localization, nuclear localization or a combination of the foregoing on the construct. The third proposed new claim recited that the construct further comprises at least two strands, wherein a first strand is a circular strand and the second strand (a) has at least one terminus, said terminus comprising a polynucleotide tail and (b) comprises two segments, wherein one segment is complementary to at least a portion of the first strand and the second segment lacks said complementarity and comprises said polynucleotide tail. There was discussion regarding further amending the claim to recite that the polynucleotide tail is hybridized to a complementary

polynucleotide sequence, wherein said complementary nucleic acid sequence comprises a non-nucleic acid entity.

E. Identification of General Thrust of Principal Arguments presented to the examiner

Amended claim 246 overcomes the prior art rejection. The proposed new claims are free of prior art. Amended claim 246 and the proposed new claims are supported by the specification.

F. A General Indication of Any other Pertinent Matters Discussed

No other pertinent matters were discussed.

G. General Results or Outcome of the Interview

Applicants agreed to submit the proposed claim amendments and new claims. Applicants agreed to point out with specificity how the claim amendments and proposed new claims overcome the prior art rejections and support for the claim amendments and new claims.

II. Obviousness-Type Double Patenting Rejection

Claims 246-252, 257-260, and 264-266 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 245-255, 257-262, 266-268, 272-280, 284-286, and 290-298 of copending Application No. 08/978,633. It is asserted that although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting application 08/978,633 claims a nucleic acid construct and composition thereof comprising a polynucleotide tail, an antibody, and a chemical modification or a ligand.

In response, Applicants note that both the instant application and application serial no. 08/978,633 are copending applications and that the nonstatutory double patent rejection is indeed provisional. Once there is an indication of allowable

subject matter in the instant application, Applicants will address the provisional double patenting rejection and if applicable, submit a Terminal Disclaimer.

II. Claim Rejections - 35 USC § 112, first paragraph

Claims 268-270 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons of record set forth in the office action mailed on 9/23/2005. It is asserted that claim 268 recites a nucleic acid construct comprising a ligand "in two or more locations on said construct." Applicants traverse the rejection and disagree with the Examiner's assertions that there is no support for these claims. It is Applicants' position that there was indeed support for new claims 268-270 in the figures (e.g., Figures 1-8). However, in order to advance prosecution, claims 268-270 have been canceled. Therefore, Applicants respectfully request that the rejections be withdrawn.

III. Claim Rejections - 35 USC §102

Four rejections under 35 USC 102 have been made. They are discussed below.

A. Craig et al.

Claims 246-252, 255, 257-260 and 264-266 are rejected under 35 U.S.C. 102(e) as being anticipated by Craig et al. (US Patent 5,766,902). The Office Action specifically states:

> Craig et al. taught methods for enhancing the targeted delivery of nucleic acid molecules to cells by coupling the nucleic acid to a ligand having affinity for a cell surface molecule or receptor. The ligand facilitates uptake of the nucleic acid by receptor mediated endocytosis (cols. 2-6). The nucleic acid molecule preferably comprises at least one transcription unit encoding a protein or RNA molecule such as an antisense oligonucleotide or ribozyme (col. 3, lines 59-62; col. 4, lines 24-28). The nucleic acid molecule may be plasmid DNA or a recombinant viral genome, such as any adenoviral or retroviral vector (col. 12, lines

1-25). Thus, the types of nucleic acids contemplated for use with the invention include single and double stranded, linear and circular, DNA and RNA molecules. The ligand may be any molecule, small or large, capable of binding to a cell and/or facilitating delivery into the cell (col. 4, lines 29-45), including proteins, carbohydrates, and metal ions. Specifically recommended are antibodies, growth factors, and fusogenic peptides (col. 4 and 8). The ligand may be chemically conjugated by covalent bonded to the nucleic acid (col. 8, lines 14-15). Covalent conjugation would necessarily result in modification of the sugar, phosphate, or nucleobase portion of one or more nucleotides of the nucleic acid. Therefore, the construct would comprise a modified nucleotide.

With regard to claim 255, the construct as claimed in claim 246 does not require a "nucleotide analog." Therefore, claim 255 further defines an optional element and does not distinguish the claimed invention from that described by Craig et al.

Similar reasoning applies to the invention defined in claims 259 and 260. Craig et al. describe at the very least natural polymeric, non-nucleic acid entities such as proteins that may be coupled to nucleic acid constructs encoding proteins and/or RNAs. Claims 259 and 260 do nothing more than further define synthetic polymers, which are optional elements of the invention claimed in claim 257.

With regard to claim 266, although Craig et al. is silent with respect to charge properties of the ligand/nucleic acid complexes, Craig et al. anticipates all of the claimed structural limitations. Moreover, proteins may, depending on the pH, carry a net negative or positive charge, which charge would supplement or offset the charge of the nucleic acid. Therefore, there is reason to believe the complexes of Craig et al. may, in some instances, be neutral.

Applicants respectfully traverse the rejection. However, in order to advance prosecution, claim 246 has been amended to recite that the claimed construct comprises at least one modified nucleotide or nucleotide analog comprising a fusogenic protein and at least one modified nucleotide or nucleotide analog comprising a ligand. Further, new claim 274, which depends from claim 246 recites

that the construct may further comprise at least one modified nucleotide or nucleotide analog that further confers nuclear localization. Applicants note that new claim 246 does not anticipate Craig. Craig merely discloses using a modified nucleotide coupled to **one** ligand. Applicants do note that Column 8 of Craig does disclose that a DNA construct may be associated with a fusogenic protein. However, there is no disclosure in Craig that a construct may contain both a fusogenic protein **and** a ligand. The use of a fusogenic protein appears to be presented only as an alternative to using other ligands. Specifically, column 8, lines 28-31 states "Delivery of the foreign DNA into the target cell may also be achieved via the DNA construct's association with an endosomal disruption agent, such as the influenza hemagglutinin fusogenic peptide". Amended claim 246 recites a construct that contains at least one fusogenic protein in conjunction with at least one ligand. Furthermore, there was no suggestion or disclosure of a construct containing at least one modified nucleotide or nucleotide analog comprising at least one fusogenic protein, at least one nucleotide or nucleotide analog comprising a ligand and further, at least one nucleotide or nucleotide analog comprising a nuclear localization signal, the subject matter recited in claim 274.

Claims 247-252 and 264-267 depend ultimately from claim 246. Thus arguments made with respect to claim 246 would apply to these claims as well.

Applicants also note that new claims 271-273 have also been added. Neither of these new claims are anticipated by Craig. As noted above, new claims 271-273 have been added to recite specific embodiments. Specifically, claim 271 recites that the construct is double stranded and that just one of the strands comprises a modified nucleotide, nucleotide analog or combination of the foregoing and that the non-nucleic acid entity is either a polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing. Claim 272 depends from claim 271. The construct disclosed in Craig would have ligands on both strands of the construct. Claim 273 recites that the construct comprises a tail and further that the tail is bound to a complementary nucleic acid sequence. The complementary nucleic acid sequence comprises non-nucleic acid entities. Craig does not disclose a construct

containing a tail.

In view of the above arguments, amendments of claim 246 and new claims 271-274, Applicants assert that the rejection over Craig has been overcome. Therefore, Applicants respectfully request that this rejection be withdrawn.

B. Low et al.

Claims 246-252, 255, and 264-270 are rejected under 35 U.S.C. 102(b) as being anticipated by Low. The Office Action specifically states:

> The claims read on biotinylated and folate-modified polynucleotides. Biotin modified nucleotides are considered to represent both "modified nucleotides" and "nucleotide analogs" absent convincing evidence to the contrary. An explicit definition clearly excluding such an interpretation is not found in the instant specification. Moreover, Low et al. claim nucleic acid analogs as part of their invention (claims 14 and 15).
>
> Low et al. taught a method for enhancing the internalization of polynucleotides into cells in vitro and in vivo, comprising the incorporation of biotin and/or folate into the polynucleotide (cols. 1-9; Examples 12, 16, 17, 21 –23, beginning at col. 12; and claims 1-27). Biotin and folate are said to promote endocytosis of the biotinylated or folate-modified polynucleotide (cols. 2-3, for example). The method can be applied to enhance the uptake of virtually any desired polynucleotide, including plasmid DNA and viral vectors, artificial chromosomes, antisense oligonucleotides, ribozymes and many other nucleic acid molecules, including retroviral genomes and transcription units (col. 3, lines 25-50; Example 12 and 16; claim 17; and see list of possible polynucleotides at col. 5). Particular examples show expression biotinylated plasmids encoding an ampicillin or kanamycin resistance gene-i.e., mRNAs. By nature, biotinylation and folate modification, according to the method taught and exemplified, would result in multiple biotins and/or folates at multiple locations in the nucleic acid molecule. Moreover, Low et al. expressly contemplate incorporating multiple molecules of biotin and folate at multiple locations in the molecule to take advantage of each type of receptor (col. 8, lines 15-40). Biotin and folate may be covalently or non-covalently linked to the polynucleotide (cols. 5,

beginning at line 58 to col. 8, line 40; and see examples cited above). End-labeling methods are also included (col. 6, bottom).

Applicants respectfully traverse the rejection. However, in order to advance prosecution, claim 246 has been amended to recite that the construct comprises at least one modified nucleotide or nucleotide analog comprising a fusogenic protein and at least one modified nucleotide or nucleotide analog comprising a ligand. Further, new claim 274, which depends from claim 246 recites that the construct may further comprise at least one modified nucleotide or nucleotide analog that comprises a nuclear localization signal. Applicants note that amended claim 246 is not anticipated by Low. Low merely discloses a method for enhanced transmembrane transport of exogenous molecules by using, e.g., biotinylated polynucleotides. There was no suggestion or disclosure of a construct comprising in addition to containing at least one modified nucleotide or nucleotide analog comprising a fusogenic protein **and** at least one nucleotide or nucleotide analog comprising a ligand, the subject matter recited in amended claim 246. Furthermore, there was no disclosure or suggestion of subject matter recited in new claim 274, a construct containing at least one modified nucleotide or nucleotide analog comprising at least one fusogenic protein, at least one nucleotide or nucleotide analog comprising a ligand and further, at least one nucleotide or nucleotide analog comprising a nuclear localization signal.

Claims 247-252, 255 and 264-267 depend ultimately from claim 246. Thus arguments made with respect to claim 246 would apply to these claims as well. Furthermore, claims 268-270 have been canceled.

Applicants also note that new claims 271-273 have been added. Neither of these new claims are anticipated by Low. Specifically, claim 271 recites that the construct is double stranded and that just one of the strands comprises a modified nucleotide, nucleotide analog or combination of the foregoing and that the non-nucleic acid entity is either a polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing. Claim 272 depends from claim 271. In contrast, in Low, a biotin is attached to a polynucleotide. There is no disclosure or suggestion in Low regarding attachment of non-nucleic acid entities such as a

polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing to a modified nucleotide or nucleic acid analog.

Claim 273 recites that the construct comprises a tail and further that the tail is bound to a complementary nucleic acid sequence. The complementary nucleic acid sequence comprises non-nucleic acid entities. In contrast, in Low, there is no teaching of a construct comprising a modified nucleic acid or nucleic acid analog comprising a non-nucleic acid entity and a tail, where the tail is hybridized to a complementary sequence **and** the complementary sequence comprises a non-nucleic acid entity.

In view of the above arguments, amendments of claim 246 and new claims 271-274, Applicants assert that the rejection over Low has been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

C. Olsen et al.

Claims 246-249, 252, 255, 267, and 268 are rejected under 35 U.S.C. 102(b) as being anticipated by Olsen. The Office Action specifically states:

> The claims read on phosphorothioated plasmid DNA such as that taught by Olsen et al.
>
> Olsen et al. taught a method for site directed mutagenesis of genes contained in plasmid DNA, comprising selective incorporation of one or more deoxynucleoside 5'-[a thio]triphosphates (see Introduction, Results, and Conclusion, pp. 1451-1455). Incorporation of phosphorothioates produces sites of nuclease resistance in the plasmid, which may be used to advantage to incorporate mismatched bases (Results? page 1452). Accordingly, Olsen et al. taught a method for producing phosphorothioate-modified plasmid DNA encoding mutant genes, i.e., mRNAs. The DNA contains both modified and unmodified nucleotides, is modified along the sugar phosphate backbone, which confers nuclease resistance.

Applicants respectfully traverse the rejection. In Applicants' view, claim 246 is not anticipated by Olsen. Olsen merely discloses phosphorothioate analogs. There was no suggestion or disclosure of a construct comprising in addition to containing at

least one modified nucleotide or nucleotide analog comprising a fusogenic protein, at least one nucleotide or nucleotide analog comprising a ligand, the subject matter recited in amended claim 246.

Claims 247-249, 252, 255, 267 and 268 depend ultimately from claim 246. Thus arguments made with respect to claim 246 would apply to these claims as well. Claim 268 has been canceled. Further, new claim 274, which depends from claim 246 recites that the construct may further comprise at least one modified nucleotide or nucleotide analog that comprises a nuclear localization signal. There is no disclosure or suggestion of such a construct.

Applicants also note that new claims 271-273 have been added. Neither of these new claims are anticipated by Olsen. As noted above, new claim 271 recites that new claims 271-273 have been added to recite specific embodiments. Specifically, claim 271 recites that the construct is double stranded and that just one of the strands comprises a modified nucleotide, nucleotide analog or combination of the foregoing and that the non-nucleic acid entity is either a polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing. Claim 272 depends from claim 271. In contrast, as noted above, Olsen discloses phosphorothioate analogs, analogs which merely confer nuclease resistance. There is no disclosure or suggestion in Olsen regarding attachment of non-nucleic acid entities such as a polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing to a modified nucleotide or nucleic acid analog that confers cell targetting.

Claim 273 recites that the construct comprises a tail and further that the tail is bound to a complementary nucleic acid sequence. The complementary nucleic acid sequence comprises non-nucleic acid entities. In contrast, in Olsen, there is no teaching of a construct comprising a modified nucleic acid or nucleic acid analog comprising a non-nucleic acid entity and a tail, where the tail is hybridized to a complementary sequence **and** the complementary sequence comprises a non-nucleic acid entity.

In view of the above arguments, amendments of claim 246 and new claims

271-274, Applicants assert that the rejection over Olsen has been overcome. Therefore, Applicants respectfully request that this rejection be withdrawn.

D. Hirsch et al.

Claims 246-249, 252, 255, 257-260, and 264-268 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirsch. The Office Action specifically states:

> Hirsch et al. taught a method for targeted transfection of plasmid DNA, comprising covalently coupling the DNA to a monoclonal antibody. In one example, the plasmid DNA encodes the neomycin resistance gene Fig. 1 and results, pp 138-9). It is said the conjugated plasmid is effectively transfected into cells and can result in stable long term expression of the encoded gene. The monoclonal antibody provides cell targeting specificity as in the case demonstrated wherein the cells transfected carried the CD3 surface antigen (Discussion, page 139). As such, it is clear Hirsch et al. teach using the method with other antibodies to selectively target a cell population based on distinctive cell surface attributes.
>
> With regard to claim 266, although Hirsch et al. is silent with respect to charge properties of the ligand/nucleic acid complexes Hirsch et al, anticipates all of the claimed structural limitations. Moreover, antibodies may, depending on the pH, carry a net negative or positive charge, which charge would supplement or offset the charge of the nucleic acid. Therefore, there is reason to believe the complexes of Hirsch et al. may, in some instances, be neutral.
>
> With regard to claim 268, the coupling method in solution used by Hirsch et al. would provide conditions suitable to the coupling of more than one antibody. There is no reason to believe the method resulted in one and only one antibody being coupled to the plasmid.

Applicants respectfully traverse the rejection. In Applicants view, amended claim 246 is not anticipated by Hirsch. Hirsch merely discloses a plasmid attached to a monoclonal antibody. There was no suggestion or disclosure of a construct comprising at least one modified nucleotide or nucleotide analog comprising a igand, **and** at least one nucleotide or nucleotide analog comprising a fusogenic protein.

Claims 247-249, 252, 255, 267 and 268 depend ultimately from claim 246. Thus arguments made with respect to claim 246 would apply to these claims as well. Claim 268 has been canceled.

Further, new claim 274, which depends from claim 246 recites that the construct may further comprise at least one modified nucleotide or nucleotide analog that comprises a nuclear localization signal. There was no disclosure or suggestion of such a construct.

Applicants also note that new claims 271-273 have been added to recite specific embodiments. Neither of these new claims are anticipated by Hirsch et al. As noted above, new claim 271 recites that new claims 271-273 have been added to recite specific embodiments. Specifically, claim 271 recites that the construct is double stranded and that just one of the strands comprises a modified nucleotide, nucleotide analog or combination of the foregoing and that the non-nucleic acid entity is either a polypeptide, protein, saccharide, fatty acid, fatty acid ester or combination of the foregoing. Claim 271 is supported by the specification in Figure 3 and on pages 36 and 126 (Example 4). Claim 272 depends from claim 271. There is no teaching in Hirsch regarding selectivley attaching the monoclonal to just one strand. Thus given that benzoquinone is used in Hirsch to attach the antibody to the plasmid, the construct in Hirsch would contain monoclonal antibodies on both strands. The method taught by Hirsch cannot avoid modifying both strands simultaneously.

Claim 273 recites that the construct comprises a tail and further that the tail is bound to a complementary nucleic acid sequence. The complementary nucleic acid sequence comprises non-nucleic acid entities. In contrast, in Hirsch, there is no teaching of a construct comprising a modified nucleic acid or nucleic acid analog comprising a non-nucleic acid entity and a tail, where the tail is hybridized to a complementary sequence **and** the complementary sequence comprises a non-nucleic acid entity.

In view of the above arguments, amendments of claim 246 and new claims 271-274, Applicants assert that the rejection over Hirsch has been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

IV. Claim Rejections - 35 USC §103

Claims 250, 251, 269, and 270 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirsch et al. (1993) *Transplantation Proceedings* 25: 138-139 ("Hirsch") as applied to claims 246-249, 252, 255, 257-260, and 264-268 above, and further in view of Keating et al. (US Patent 6,503,755) ("Keating") and Bos et al. (1992) *Hybridoma* 11: 41-51 ("Bos"). The Office Action asserts:

> .... it would have been obvious to one of skill at the time of invention to combine the antibody-mediated transfection method of Hirsch et al. with the linearization technique of Keating et al. or Bos et al. to further enhance the cell targeting and uptake of the plasmid DNA. The methods could have been combined with no significant or apparent change in their respective functions, wherein the antibody provides for cell targeting specificity and the linearization provides for enhanced uptake. Stated another way, it would have been obvious to apply the techniques of Keating et al. or Bos et al. to the antibody-coupled plasmids of Hirsch et al. to produce a linearized, antibody-conjugated plasmid with predictable properties.
>
> The methods complement one another. As a result, the combination would have combined the benefits taught individually by Hirsch et al., Keating et al., and Bos et al. It would be the normal desire of any scientist in the field to achieve optimal transfection efficiency in the target cell population by applying those techniques, singly or in combination, known in the prior art to enhance plasmid DNA transfection.

Applicants respectfully traverse the rejection. Claims 250 and 251 depend from claim 246. As noted above, in order to advance prosecution, claim 246 has been amended to recite that the construct comprises at least one modified nucleotide or nucleotide analog comprising a fusogenic protein and at least one modified nucleotide or nucleotide analog comprising a non-fusogenic protein ligand. There was no suggestion in any of the cited references regarding such a construct and certainly no suggestion of such a construct comprising a polynucleotide tail. The construct in Hirsch is merely attached to a monoclonal antibody.

Keating and Boz would not add anything of signficance to Hirsch. Keating merely discloses transfecting cells attached to a support with polynucleotides. In Keating, transfection efficiency is reported to be enhanced by attachment of cells to particles and optionally linearizing plasmids, not by modifying nucleotides. Nucleotides in Keating are only modified for detection purposes. Bos merely teaches that plasmid transfection efficiency can be increased by electroporation and possibly linearization. There was no discussion in Bos regarding modifying nucleotides to increase transfection efficiency. At best, the combination of Hirsch with Keating and Bos would teach a linearized plasmid covalently attached to a monoclonal antibody, a non-fusogenic protein ligand. Thus the combination of Hirsch, Keating and Bos omits a critical element, the second non-nucleic acid entity, a fusogenic protein. Applicants note that the other claims, claims 269-270 have been canceled.

It is Applicants position that the new claims 271-274 are not obvious in view of the cited references. As noted above, in the construct of Hirsch, monoclonal antibodies would be attached to both strands of the construct. Thus, at best the combination of Hirsch and Keating and Boz would teach a linearized plasmid where the monoclonal antibody is attached to the plasmid on both strands. Clearly, essential elements of claims 271-273 have been omitted, a ligand such as a monoclonal antibody attached to just one strand (claim 271) and a ligand such as a monoclonal antibody attached to a strand complementary to a polynucleotide tail (claim 273). New claim 274, which depends from claim 246 and further includes a third non-nucleic acid entity, a nuclear localization signal would also not be obvious over Hirsch in view of Keating and Boz.

In view of the above arguments and amendments of claim 246, Applicants assert that the rejections under 35 USC 103 have been overcome. Therefore, Applicants respectfully request that the rejections be withdrawn.

V. Summary and Conclusions

Claims 246-252, 255, 257-260 and 264-270 are pending in the application. Claims 257-260 and claims 268-270 have been canceled without prejudice. Claim

246 has been amended to more distinctly claim that which Applicants regard as their invention. Applicants assert that the amendment of claim 246 and cancellation of 257-260 and 268-270 have obviated the rejections. Claims 271-274 have been added.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney request that he be contacted at (914) 712-0093.

Respectfully submitted,

/Cheryl H Agris/

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